52 42

CLAIMS

1. An isolated specific binding member capable of binding an intracellular antigen, wherein said specific binding member comprises a polypeptide binding domain comprising an amino acid sequence substantially as set out as residues 99 to 106 of SEQ ID NO:2.

2. An isolated specific binding member according to claim 1 which further comprises the polypeptide binding domains substantially as set out as residues 31-36 and 51-66 of SEQ ID NO:2.

3. An isolated specific binding member according to claim 2 wherein said binding domains are carried by a human antibody framework.

4. An isolated specific binding member according to claim 3 which comprises substantially the polypeptide sequence of SEQ ID NO:2.

5. An isolated specific binding member capable of binding an intracellular antigen, wherein said specific binding member comprises a polypeptide binding domain comprising an amino acid sequence substantially as set out as residues 88 to 98 of SEQ ID NO:4.

6. An isolated specific binding member according to claim 5 which further comprises the polypeptide binding domains substantially as set out as residues 23-33 and 49-55 of SEQ ID NO:4.

7. An isolated specific binding member according to claim 6 wherein said binding domains are carried by a human

antibody framework.

8. An isolated specific binding member according to claim 7 which comprises substantially the polypeptide sequence of SEQ ID NO:4.

9. A specific binding member which comprises a first specific binding member as defined in any one of claims 1 to 4 in association with a second specific binding member as defined in any one of claims 5 to 8.

10. A specific binding member according to claim 9 in the form of an antibody F(ab')2 or scFv fragment.

11. A specific binding member according to any one of claims 1 to 10 which carries a detectable or functional label.

12. An isolated nucleic acid which comprises a sequence encoding a specific binding member as defined in any one of claims 1 to 11.

13. A method of preparing a specific binding member as defined in any one of claims 1 to 11 which comprises expressing the nucleic acid of claim 12 under conditions to bring about expression of said binding member, and recovering the binding member.

14. A specific binding member according to any one of claims 1 to 11 for use in a method of treatment or diagnosis of the human or animal body.

15. A method of preparing a specific binding member capable of binding an intracellular antigen, which method comprises:

a) providing a starting repertoire of nucleic acids encoding a VH domain which lack a CDR3 encoding

54 44

region;

b) combining said repertoire with a donor nucleic acid encoding an amino acid sequence substantially as set out as residues 99 to 106 of SEQ ID NO:1 such that said donor nucleic acid is inserted into the missing CDR3 region, so as to provide a product repertoire of nucleic acids encoding a VH domain;

c) expressing the nucleic acids of said product repertoire; and

d) selecting a specific binding member which has a maximum tumour:blood localisation ratio in a test animal of > 3:1 and optionally at said ratio an organ to blood ratio of < 1:1; and

e) recovering said binding member or the nucleic acid encoding it.

16. A method of treatment of a tumour in a human patient which comprises administering to said patient an effective amount of a specific binding member as defined in any one of claims 1 to 11.